

What is claimed is:

1. A stable, isolated cell comprising a construct with a promoter operably linked to a polynucleotide encoding a polypeptide having a biological activity of a promiscuous  $\text{G}\alpha$  protein.
2. The cell of claim 1, wherein said promoter is an inducible promoter.
3. The cell of claim 2, wherein said construct permits expression in a mammalian cells.
4. The cell of claim 1, wherein said polynucleotide has a nucleotide sequence with at least 70% sequence identity to a nucleotide sequence selected from the group consisting of the nucleotide sequence of  $\text{G}\alpha_{16}$ , SEQ ID NO: 1, the nucleotide sequence of  $\text{G}\alpha_{15}$ , and SEQ ID NO.2.
5. The cell of claim 4, wherein said polynucleotide has a nucleotide sequence selected from the group consisting of the nucleotide sequence of a  $\text{G}\alpha_{16}$  (SEQ ID NO: 1) and the nucleotide sequence of a  $\text{G}\alpha_{15}$  (SEQ ID NO:2).
6. The cell of claim 2, wherein said inducible promoter comprises a promoter operably linked to a tet operator.
7. The cell of claim 6, wherein the inducible promoter comprises a cytomegalovirus promoter.
8. The cell of claim 1, further comprising a second construct comprising a reporter gene operably linked to a second promoter, and said second promoter is modulated by a promiscuous  $\text{G}\alpha$  protein.
9. The cell of claim 8, wherein the reporter gene encodes a reporter selected from the group consisting of luciferase, green fluorescent protein, chloramphenicol acetyl transferase,  $\beta$ -galactosidase, alkaline phosphatase,  $\beta$ -lactamase, and human growth hormone.
10. The cell of claim 8, wherein said second promoter comprises a calcium-responsive promoter.
11. The cell of claim 10, wherein said calcium-responsive promoter comprises a nuclear factor of activated T cells promoter.
12. The cell of claim 11, wherein the reporter gene encodes  $\beta$ -lactamase.
13. The cell of claim 8, wherein said second promoter comprises a protein kinase C- responsive promoter.
14. The cell of claim 13, wherein the reporter gene encodes  $\beta$ -lactamase.

15. The cell of claim 1, wherein said cell further comprises a G-protein coupled receptor (GPCR).

16. The cell of claim 16, wherein said cell further comprises a polynucleotide encoding a GPCR and not naturally occurring in said cell.

17. The cell of claim 8, wherein said cell further comprises a polynucleotide encoding a GPCR and not naturally occurring in said cell.

18. An isolated cell comprising a construct with a calcium-responsive promoter operably linked to a polynucleotide encoding a reporter gene, wherein said isolated cell expresses a target protein, said calcium-responsive promoter is modulated by said target protein and with the proviso that if the function of said target protein is known, said cell is exposed to a test chemical not previously known to bind to said target protein.

19. The isolated cell of claim 18, further comprising a second polynucleotide encoding a polypeptide having a biological activity of a promiscuous G $\alpha$  protein and said second polynucleotide does not naturally occur in said cell.

20. The isolated cell of claim 19, further comprising a third polynucleotide encoding a target protein and said third polynucleotide does not naturally occur in said cell.

21. The isolated cell of claim 20, wherein said target protein has a biological activity of a GPCR.

22. The isolated cell of claim 20, wherein said target protein has a biological activity of a protein selected from the group of a transcription factor, kinase, ion channel, phosphatase, phospholipase and adenyl cyclase.

23. The isolated cell of claim 20, further comprising a chemical known to bind to said target protein.

24. The isolated cell of claim 21, further comprising a chemical selected from the group of a phorbol ester, thapsigargin, ionomycin and a kinase inhibitor.

25. The isolated cell of claim 21, further comprising a chemical, other than a chemical in normally found in a tissue culture media, not known to bind to said target protein.

26. The isolated cell of claim 21, further comprising a cell compatible media and said chemical is at a concentration of one micromolar or less in said cell compatible media.

27. A method of identifying a GPCR for a given ligand, the method comprising:

(i) expressing a putative GPCR in a cell of claim 1 or 18;

(ii) contacting said cell with a ligand; and

(iii) detecting reporter gene expression.

28. The method of claim 27, wherein said detecting comprises fluorescence detection.

29. The method of claim 28, further comprising contacting said cell with a reporter gene substrate.

30. The method of claim 27, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

31. The method of claim 30, wherein said compound is selected from the group consisting of ionomycin and thapsigargin.

32. The method of claim 30, further comprising contacting said cell with phorbol myristate acetate or an analog thereof.

33. A method of identifying a ligand for a GPCR, the method comprising:

- expressing a GPCR in a cell of claim 1 or 18;
- contacting said cell with a test chemical; and
- detecting a signal with a signal transduction detection system.

34. The method of claim 33, further comprising comparing a signal from a first plurality of cells in the presence of said test chemical with either:

- a signal from a second plurality of cells in the presence of said test chemical, wherein said second plurality of cells lack either a promiscuous G $\alpha$  protein, a target protein or a reporter gene, or
- a signal from a plurality of cells in the absence of said test chemical, wherein said plurality of cells are substantially the same as said first plurality of cells.

35. The method of claim 34, wherein said detecting comprises fluorescence detection.

36. The method of claim 35, wherein said cell comprises a dye.

37. The method of claim 36, wherein said detecting comprises reporter gene detection.

38. A method for identifying a modulator of signal transduction in a cell, the method comprising:

- contacting a cell of claim 1 or 18 with a test chemical;
- contacting said cell with a ligand that, in the absence of the test chemical, activates signal transduction in said cell, and
- detecting a signal with a signal transduction detection system

39. A method for identifying modulators of signal transduction in a cell, the method comprising:

- contacting a cell of claim 1 or 18 with a compound that directly activates a G subunit encoded by a polynucleotide,
- contacting said cell with a test chemical, and
- detecting a signal with a signal transduction detection system, wherein said signal transduction detection system comprises a reporter gene as a measure of signal transduction in said cell.

40. The method of claim 39, wherein said compound is selected from the group consisting of mastoparan and aluminum fluoride.

41. A method for identifying a GPCR for a given ligand or method of identifying a modulator of a GPCR, the method comprising:

- expressing a putative GPCR or a GPCR of known function in a cell of claim 1 or 18;
- contacting said cell with a test chemical or a ligand known to be a GPCR; and
- detecting a calcium level within said cell.

42. The method of claim 41, further comprising contacting said cell with intracellular calcium indicator and detecting fluorescence from said cell.

43. A kit comprising assay reagents and a container containing a cell of claim 1 or 18.

44. A stable, isolated cell comprising a construct with a promoter operably linked to a polynucleotide encoding a polypeptide having a biological activity of a promiscuous G $\alpha$  protein.

45. The cell of claim 44, wherein said promoter is a CMV promoter.

46. The cell of claim 44, wherein said construct permits expression in a mammalian cells.

47. The cell of claim 46, wherein said polynucleotide has a nucleotide sequence with at least 70% sequence identity to a nucleotide sequence selected from the group consisting of the

nucleotide sequence of  $\text{G}\alpha_{16}$  SEQ ID NO: 1, the nucleotide sequence of  $\text{G}\alpha_{15}$ , and SEQ ID NO.2.

48. The cell of claim 47, wherein said polynucleotide has a nucleotide sequence selected from the group consisting of the nucleotide sequence of a  $\text{G}\alpha_{16}$  (SEQ ID NO: 1) and the nucleotide sequence of a  $\text{G}\alpha_{15}$  (SEQ ID NO:2).
49. The cell of claim 44, further comprising a second construct comprising a reporter gene operably linked to a second promoter, and said second promoter is modulated by a promiscuous  $\text{G}\alpha$  protein.
50. The cell of claim 49, wherein the reporter gene encodes a reporter selected from the group consisting of luciferase, green fluorescent protein, chloramphenicol acetyl transferase,  $\beta$ -galactosidase, alkaline phosphatase,  $\beta$ -lactamase, and human growth hormone.
51. The cell of claim 50, wherein said second promoter comprises a calcium-responsive promoter.
52. The cell of claim 51, wherein said calcium-responsive promoter comprises a nuclear factor of activated T cells promoter.
53. The cell of claim 52, wherein the reporter gene encodes  $\beta$ -lactamase.
54. The cell of claim 51, wherein said second promoter comprises a protein kinase C- responsive promoter.
55. The cell of claim 54, wherein the reporter gene encodes  $\beta$ -lactamase.
56. The cell of claim 44, wherein said cell further comprises a G-protein coupled receptor (GPCR).
57. The cell of claim 56, wherein said cell further comprises a polynucleotide encoding a GPCR and not naturally occurring in said cell.
58. The cell of claim 54, wherein said cell further comprises a polynucleotide encoding a GPCR and not naturally occurring in said cell.
59. The cell of claim 58, wherein said cell arises from a cell line subjected to functional cells analysis with a signal transduction detection system.
60. A method of identifying a ligand for a GPCR, the method comprising:

- a) contacting a cell with a test chemical, wherein said cell is expressing a GPCR and arises from a cell line subjected to functional cell analysis with a signal transduction detection system; and

- b) detecting a signal with a signal transduction detection system.

61. A method for identifying modulators of signal transduction in a cell, the method comprising:

- a) contacting a cell with a compound that directly activates a  $G\alpha$  protein encoded by a polynucleotide, wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system,

- b) contacting said cell with a test chemical, and

- c) detecting a signal with a signal transduction detection system, wherein said signal transduction detection system comprises a reporter gene as a measure of signal transduction in said cell.

62. A method for identifying a GPCR for a given ligand or method of identifying a modulator of a GPCR, the method comprising:

- a) expressing a putative GPCR or a GPCR of known function in a cell, wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system;

- b) contacting said cell with a test chemical or a ligand known to be a GPCR; and

- c) detecting a calcium level within said cell.

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